

**REMARKS**

Claims 1-4, 11 and 12 were pending in the application. Claims 1 and 2 have been amended by the amendments presented herein. Support for the amendments to the claims can be found in the specification and claims as originally filed. Accordingly, after the amendments presented herein have been entered, claims 1-4, 11 and 12 will remain pending. No new matter has been added.

***Response to Examiner's Non-Responsive Amendment***

The Examiner has rejected the last amendment as presenting subject matter that is outside the group originally elected. Applicants disagree. Applicants elected the group corresponding to determining the prostate cancer status. Applicants' specification specifically teaches that determining if a subject has prostate cancer is a form of determining a subject's prostate cancer status. See for, example, page 16, line 17-23.

Accordingly, Applicants believe that there is no additional search required. In the interest of advancing prosecution, Applicants have amended the claims to indicate that the claimed methods are for determining the prostate cancer status of a subject.

Applicants address the remaining rejections in the previous office action in view of these claim amendments.

***Rejection of Claims 1-4, 11 and 12 Under 35 USC 112, Second Paragraph***

The Examiner had previously rejected claims 1-4, 11, and 12 under 35 USC 112, second paragraph as being indefinite over the use of the terms "prostate cancer status". Applicants specification is clear in the meaning of the term.

The application sets forth:

In particular, the panel of biomarkers: (Panel 3) with 90% sensitivity and 95% specificity can be used to select prostate cancer patients for surgery; Panel 1 with 92% sensitivity and 90% specificity can be used for the screening of prostate cancer in a healthy population of men and Panel 2

with 80% sensitivity and 77% specificity can be used for the diagnosis of prostate cancer and differentiate cancer from BPH.

(See page 16, lines 17-21 of the specification.)

Accordingly, based on the specification, one of skill in the art would understand the term to mean using the levels of the biomarkers of the invention to select prostate cancer patients in need of surgery; for screening for prostate cancer in a healthy population of men; and for the diagnosis of prostate cancer and differentiate cancer from BPH in a subject.

Accordingly, Applicants believe that the foregoing rejection has been rendered moot and respectfully requests withdrawal of the rejection.

***Rejection of Claim 4 Under 35 USC 112, Second Paragraph***

The Examiner has rejected claim 4 under 35 USC 112, second paragraph as being indefinite because, allegedly, the metes and bounds of the claimed subject matter are not clear. Applicants respectfully traverse.

The Examiner alleges that the claim is unclear if the practitioner selects to manage treatment by taking no further action. Applicants disagree. The claims, as amended, are directed to methods for determining prostate cancer status. A clinician of ordinary skill in the art would find the claims to be clear and definite as pending. It would be clear to a clinician that if a subject is determined not to have cancer that the appropriate way to manage the subject is by "taking no further action".

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

***Rejection of Claims 1-5, 11 and 12 Under 35 USC 112, First Paragraph***

The Examiner has rejected claims 1-5, 11 and 12 under 35 USC 112, first paragraph as not being enabled. While in no way acquiescing to the validity of the Examiner's rejection, and solely in the interest of expediting prosecution, Applicants have amended the claims to be directed to methods for determining prostate cancer

status by measuring the amount of Marker I in a sample, wherein a decrease in the amount of the marker as compared to a control is indicative that the subject has prostate cancer.

The Examiner indicates in the Office Action that the specification teaches an association between an abnormal level of Biomarker I in a sample and the presence of prostate cancer. Accordingly, the claims as amended are enabled by the specification as filed.

Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

***Rejection of Claims 1-5, 11 and 12 Under 35 USC 102(a)***

The Examiner has rejected claims 1-5, 11, and 12 under 35 USC 102(a) as being anticipated by Tsuneki et al. Applicants respectfully traverse this rejection.

As indicated above, Applicants are entitled to the benefit of the PCT and the US provisional application. Accordingly, the priority date to which the instant application is entitled is April 26, 2002. Tsuneki et al. was published in 2004, clearly after the priority date of the instant invention. Accordingly, Tsuneki et al is not available as art against the pending claims.

Moreover, even if *arguendo* Tsuneki et al. was available as art, against the pending claims are patentable over this reference. Tsuneki et al. does not teach or suggest a biomarker that is at least 7808 kDa and correlated with prostate cancer status, e.g., the presence or absence of prostate cancer.

***Rejection of Claims 1-5, 11 and 12 Under 35 USC 102(a)***

The Examiner has rejected claims 1-5, 11, and 12 under 35 USC 102(a) as being anticipated by Gretzer et al. Applicants respectfully traverse this rejection.

As indicated above, Applicants are entitled to the benefit of the PCT and the US provisional application. Accordingly, the priority date to which the instant application is

entitled is April 26, 2002. Gretzer et al. was published in 2004, clearly after the priority date of the instant invention. Accordingly, Gretzer et al. is not available as art against the pending claims.

Moreover, even if *arguendo* Gretzer et al. was available as art, the pending claims are patentable over this reference. Gretzer et al. does not teach or suggest a biomarker that is at least 7.808 kDa and correlated with the presence or absence of prostate cancer. The Examiner indicates that Gretzer teaches a biomarker that is 9 kDa and that "9 kDa is about 7.808 kDa". Applicants respectfully disagree.

As the Examiner indicates in the office action, Applicants define the term "about" as used in the application. "About", when referring to the mass of the biomarkers, is defined to include the variances in mass accuracy and in the operation of the instrument. The definition at paragraph [0017] defines the variances to be within 0.15% of the actual mass value. Accordingly, based on the teachings in the specification, biomarkers that are "about" 7.808 kDa will have molecular weights that range from 7.796 kDa to 7.820 kDa. Clearly, 9 kDa is not within the range that is "about" 7.808 kDa.

#### ***Rejection of Claims 1-5, 11 and 12 Under 35 USC 102(b)***

The Examiner has rejected claims 1-5, 11, and 12 under 35 USC 102(b) as being anticipated by Cazares et al. Applicants respectfully traverse this rejection.

The Examiner alleges that Cazares et al. teach biomarkers that are about 7.808 kDa. Specifically, the Examiner indicates that Cazares et al. teach biomarkers that are about 6.913, 7.368, and 8.238 kDa. For the reasons indicated above, these biomarkers are not "about" 7.808 kDa.

As indicated above, Applicants define the term "about" as used in the application. "About", when referring to the mass of the biomarkers, is defined to include the variances in mass accuracy and in the operation of the instrument. The definition at paragraph [0017] defines the variances to be within 0.15% of the actual mass value. Accordingly, based on the teachings in the specification, biomarkers that are "about"

7.808 kDa will have molecular weights that range from 7.796 kDa to 7.820 kDa. Clearly, biomarkers that have masses of 6.913, 7.368, and 8.238 kDa are not within the range that is "about" 7.808 kDa.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

**Conclusion**

In view of the above arguments and amendments, Applicants believe the pending application is in condition for allowance. If a phone call with the Applicant's attorney would help to expedite prosecution, the Examiner is urged to contact the undersigned.

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Respectfully submitted,

By: 

Jonathan M. Sparks, Ph.D.

Registration No.: 53,624

EDWARDS ANGELL PALMER & DODGE  
LLP

P.O. Box 55874

Boston, Massachusetts 02205

(617) 517-5543

Attorneys/Agents For Applicant